

The logo for the BIG Health Consortium is positioned in the upper left. It features the word "BIGHEALTH" in a bold, dark blue font, with "CONSORTIUM™" in a smaller, grey font below it. The background is a light blue gradient with a faint grid of binary code (0s and 1s) and a large, stylized graphic of a globe or sphere composed of horizontal and vertical lines, with several thick, dark blue horizontal bands crossing it.

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***“Linking Research and Care to Make
Personalized Medicine a Reality”***

BIG Health Consortium™ Overview

Presented by Ken Buetow, Ph.D.

March 19, 2009

- **Purpose:** To introduce a new endeavor called the BIG Health Consortium™ that seeks to transform the biomedical enterprise by unifying research and care
- **Outline:**
 - The Challenges
 - The Opportunities
 - A Systems Approach: BIG Health Consortium™
 - BIG Health in Action

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Biomedicine: The Challenges

Three Levels of Challenges

- At the “Micro” level:
 - Health care is costly for individuals, and the care they receive is often ineffective or harmful
- At the “Macro” level:
 - Target discovery and validation is expensive, and often leads to blind alleys
 - Rx development is facing increasing costs and difficulty, and declining productivity
- At the “Eco(system)” level:
 - The health care system is dysfunctional, with multiple perverse incentives along the discovery>delivery continuum
 - The demographics and disease trends suggest an approaching perfect storm

At each level, there are “disconnects” that cause major problems

The Biomedical Landscape at the “Eco” Level

- Isolated information “islands”
- Information dissemination uses models recognizable to Gutenberg
- Pioneered by Royal Academy of Science of London in the 17th century
 - Write manuscripts
 - “Publish”
 - Exchange information at meetings



Information “Disconnects” are found throughout the Eco Level



Basic Research	Clinical/Translational Research	Health Care Delivery
Huge amounts of data from countless sources	Expiring patents, development and regulatory delays; post-marketing product recalls	Clinical data from disparate sources difficult to integrate; hard to track patients across sites and over time
Dramatically increasing costs and declining resources	Dramatically increasing costs of clinical development; slow/difficult recruitment process for clinical trials	Rising costs; inadequate reimbursement
Lack of data sharing leads to redundancy and lack of productivity	Countless biomarker targets, but difficult to validate clinically for drug development	Lack of data sharing leads to redundancy, lack of productivity; little ability to improve care based on previous trials
Continued organizational and data “disconnects” slow the time to discovery	Continued organizational and data “disconnects” slow the time to translate research findings into safe and effective products	Continued organizational and data “disconnects” slow the time to translate clinical research findings into better clinical care

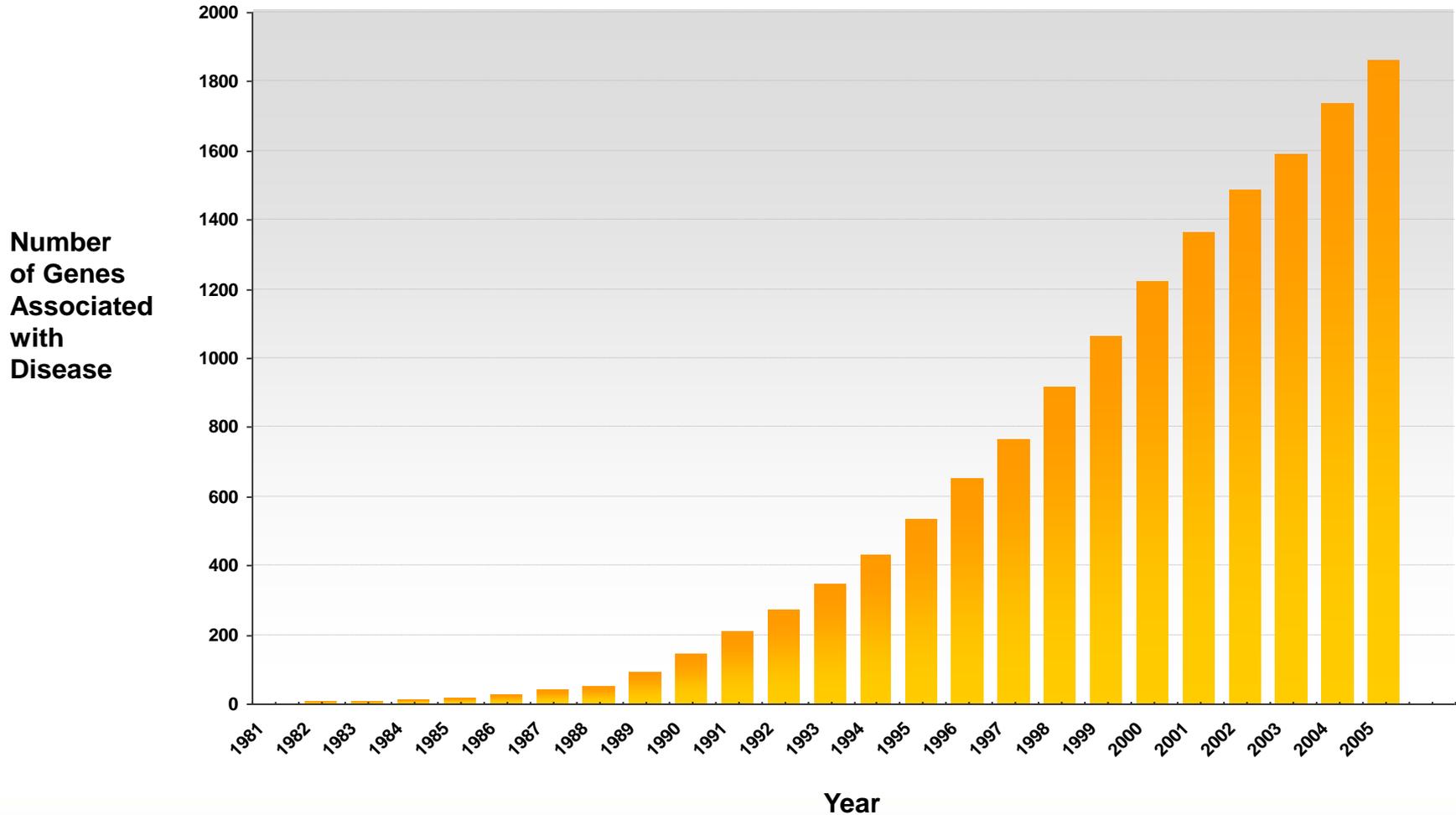
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Biomedicine: The Opportunities

Scientific Understanding is Increasing Dramatically...



Cumulative Pace of Disease Gene Discovery 1981-2005



Source: Online Mendelian Inheritance in Man

Basic Discoveries are Increasingly Linked to Clinical Relevance



Glioblastoma study (Nature, September 2008)

- Performed in-depth, integrated characterization of the tumor genomes of 206 GBM patients
- Identified three genes and three core biological pathways commonly altered in GBM tumors
- Revealed possible mechanism by which GBM tumors become resistant to standard chemotherapy

Liver cancer study by Hoshida et al. (NEJM, October 2008)

- Developed method to perform genomic analyses on tissue samples preserved with formalin (standard method used by tissue archives for last 100 years, not amenable to genomic study)
- Could unlock genomic information contained in millions of archived samples around the world
- Used method to identify gene signature predictive of recurrence in liver cancer (3rd most lethal cancer worldwide, has 70% recurrence rate)

New Genomics-guided Dx/Rx Products Are Emerging



Table 2 A growing personalized medicine cabinet

Drug/indication	Drug developer	Test/selected product developers	Comments
Testing required by FDA			
Erbix/colon cancer	Imclone	EGFR pharmDX/DAKO Cytomation	IHC to determine EGFR presence or absence. Test also recommended, but not required, for use with Erbix in head and neck cancer
Selzentry/HIV AIDS	Pfizer	Trofile (CCR5 tropism)/ Monogram Biosciences	Amplification of patient HIV genome, creation of artificial viral particles and infection assay
Vectibix ^a /colon cancer	Amgen	EGFR expression KRAS/DxS	The test is required in Europe. KRAS mutations may be relevant in a variety of other cancers
Herceptin/breast cancer	Genentech/Roche	HER2 overexpression/variou	Can be done by FISH or IHC but apparently variation in accuracy is possible between labs. Test also useful for prescribing GSK's Tykerb (lapatinib)
Testing recommended by FDA			
Imuran (azathioprine)/autoimmune diseases and transplants	GSK	Thiopurine methyltransferase variants/variou	Enzyme activity and/or genotyping
Tegretol (carbamazepine)/epilepsy and bipolar disorder	Various	HLA-B 1502 variant found in people of Asian ancestry/variou	Boxed warning recommends that patients with Asian ancestry receive a genetic test before starting treatment, because their risk of serious adverse reactions is 10 times that (1 to 6 per 10,000) of European ancestry
Tarceva (erlotinib)/NSCLC	Genentech/OSI	EGFR pharmDX/DAKO Cytomation	Impact of testing on treatment still unclear because too few patients were tested in trials
Camptosar (irinotecan)/colon cancer	Pfizer	UTG1A1 variants/Third Wave	Third Wave has a marketing relationship with Genzyme Genetics for this test
Elitek (rasburicase)/cancer	Sanofi-Aventis	G6PD deficiency/variou	Beutler fluorescent-spot test
Coumadin/anticoagulant	Various	CYP2C9 and VKOR (vitamin K epoxide reductase) variant genotyping/Clinical Data, Genelex (Seattle) and Roche	There is much debate about whether and how to test

Selected drugs for which informational tests are available

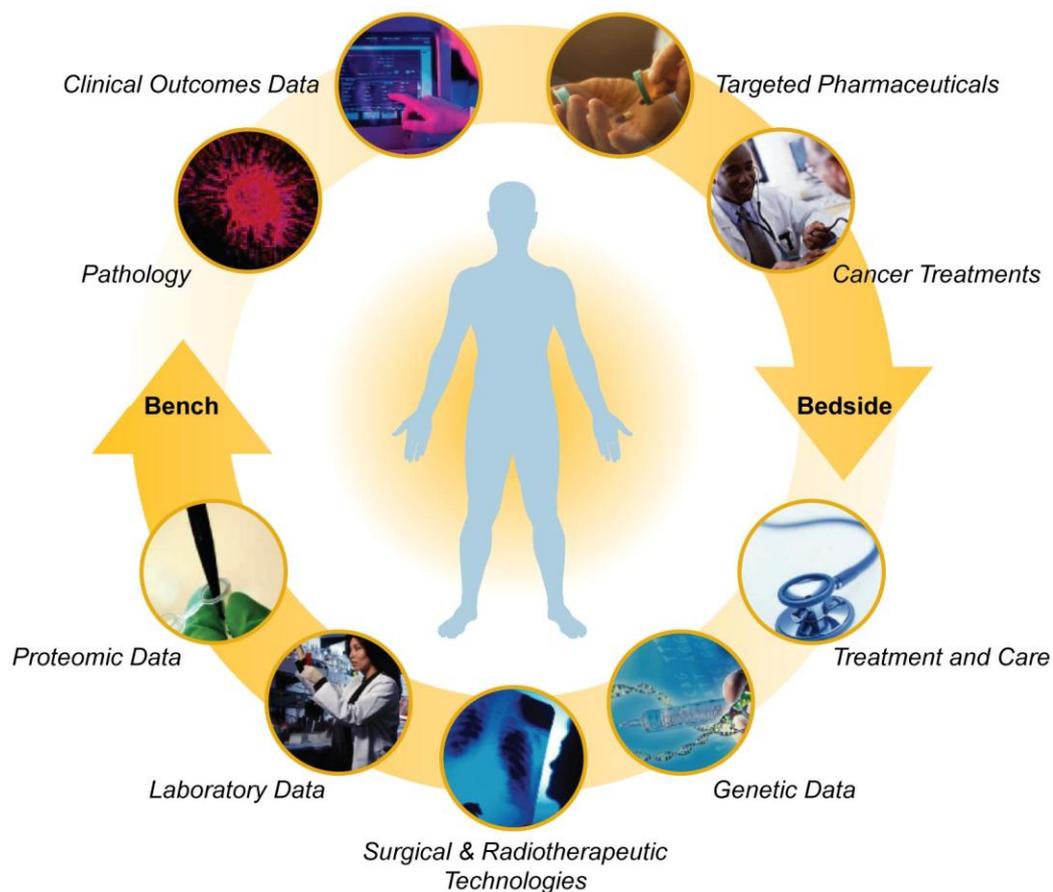
Zigen (abacavir)/HIV AIDS	GSK	HLA-B 5701b/variou	Predictive value for hypersensitivity reaction
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A Systems Approach: BIG Health Consortium™

*“The world we have created today has problems which cannot be solved by thinking the way we thought when we created them.”**

**Albert Einstein*

Personalized Medicine



- **Predictive, Preemptive, Participatory.....**
- **Unifies** clinical research, clinical care, and discovery (bench-bedside-bed) into a seamless continuum
- **Results** in improved clinical outcomes
- **Accelerates** the time from discovery to patient benefit
- Enables a health care **system**, not a disparate “sector”
- **Empowers** consumers in managing their health over a lifetime

Definition:

Use of an individual's characteristics (and characteristics of his or her disease) to help identify which of many intervention alternatives should be utilized to maximize a health outcome.

New Model: Link Discovery > Clinical Research > Clinical Care



The Concept: **Connect scientific discovery, clinical research and clinical care into a seamless continuum that continually builds and applies knowledge**

The opportunity for research:

- **Faster, more efficient patient recruitment for trials**
- **Improved clinical trials outcomes due to improved patient selection**
- **Faster adoption by the health care delivery system**
- **Reduced infrastructure costs**

The opportunity for health care providers:

- **A pathway to innovation**
- **A strategy to address clinical care challenges to improve outcomes**
- **A chance for physicians outside academic medical centers to participate in clinical research**
- **Additional resource source**

Pediatric cancer is a successful example of this approach

New Model: Link

Discovery > Clinical Research > Clinical Care



Tremendous improvement in childhood cancer survival since 1975

- **Overall reduction of cancer mortality by 50%**
- **acute lymphoblastic leukemia survival rate has improved from 5% in the 1960's to more than 85%**
- **Molecular characterization used to determine treatment**

Childhood cancer is treated in a context that blends care delivery and clinical research

- **Researchers and practitioners are able to correlate experimental laboratory data with clinical data (treatment, history, pathology, outcome, etc.)**
- **Clinical data are utilized to continuously evaluate outcomes**
- **Researchers develop and refine evidence-based strategies at an individualized level**
- **Care providers improve quality by adherence to care standards**

**Information flow is critical...
this model cannot be achieved without IT connectivity**

Vision:

A biomedical system that synergizes the capabilities of the entire community to realize the promise of personalized medicine

Mission:

The BIG Health Consortium™ is a collaboration among stakeholders in biomedicine, including *government, academe, industry, non-profit, and consumers*, who come together in a novel organizational framework *to demonstrate the feasibility and benefits of the personalized medicine paradigm.*

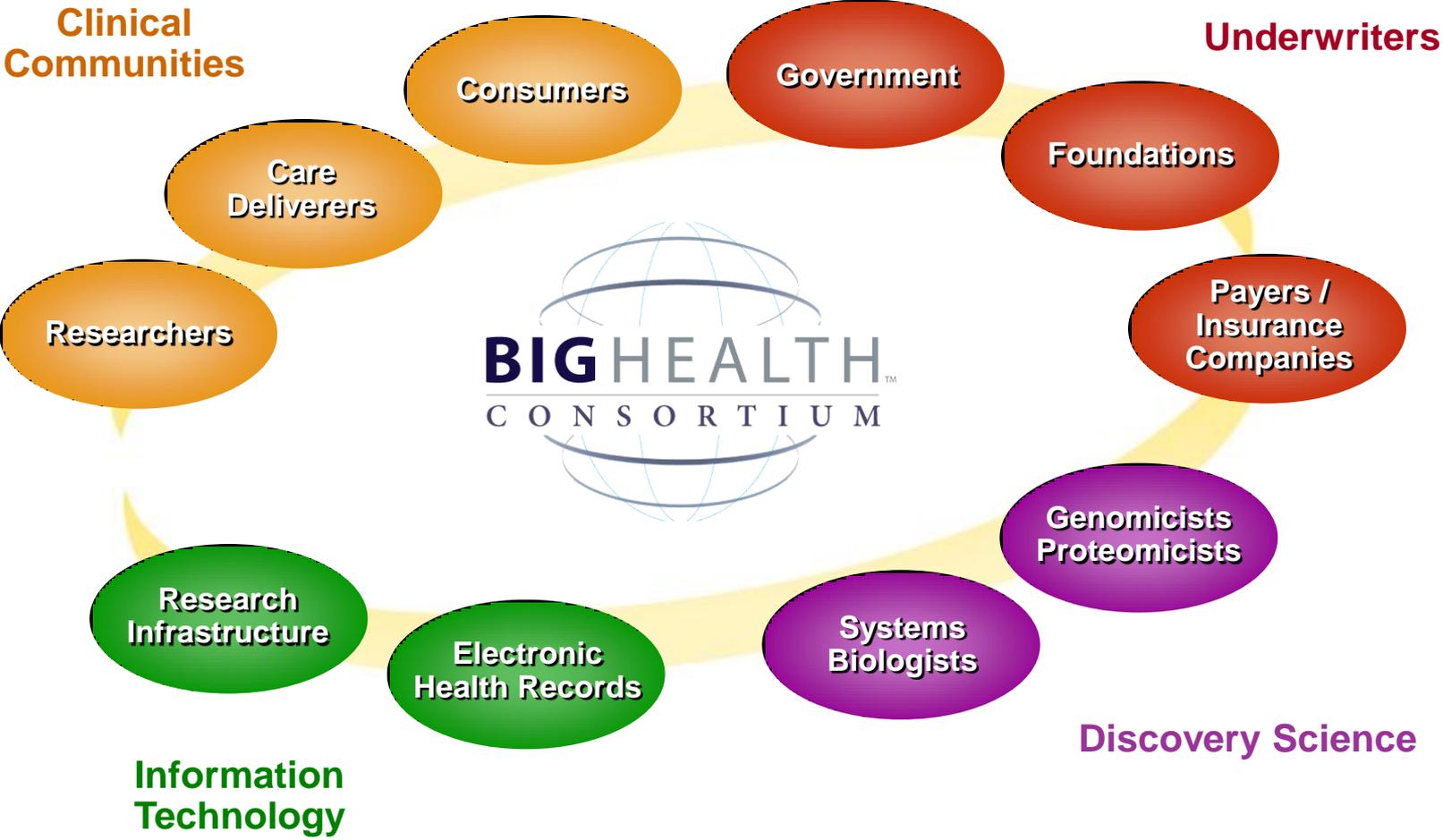
Strategy:

Through a series of personalized medicine **Projects**, with an expanding number of collaborators, BIG Health will **bootstrap** a new approach in which clinical care, clinical research, and scientific discovery are linked.

BIG Health will demonstrate that:

- Loosely-coupled sectors within life sciences and health care can come together in an ecosystem to implement personalized medicine real-world projects, in real time.
- The tools, infrastructure and standards of NCI's informatics infrastructure (caBIG[®]), as well as other IT capabilities, can be applied to linking this ecosystem.
- Such an ecosystem can be financially self-sustaining.
- ***Clinical care, clinical research, and scientific discovery can be connected in a seamless continuum that speeds innovation and benefits patients.***

BIG Health Ecosystem



BIG Health In Action

“21st Century medicine requires new organizational approaches that embrace our capacity to work digitally...”





Research



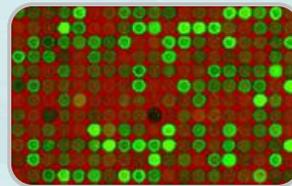
Participants

Patients join research networks, grant consent, agree to be “sought” and to enroll – “on-demand” participants



Biospecimen Collections

Researchers can access and query large collections of well-characterized, clinically annotated specimens



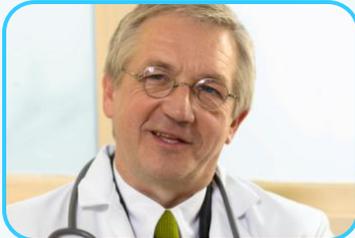
Discovery of Correlations

Biomarkers are identified and validated; disease sub-groups emerge



Individualization of Treatment

Patients are identified by sub-groups and treated appropriately



Clinical Practice



Electronic Health Records

EHRs can connect to clinical trials in hospital settings



Research Finding Knowledgebases

Large-scale databases of latest research findings are connected to health delivery encounter

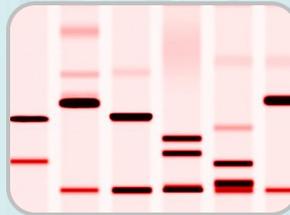


Learning Healthcare System

Local and national clinical encounter information is fed back to care providers to help inform clinical decision making



Consumer



My Genomic Profile

Consumers get their genetic and predisposition risk information



My Prevention Strategies

Consumers work with genetic counselors; coordinate with health care provider



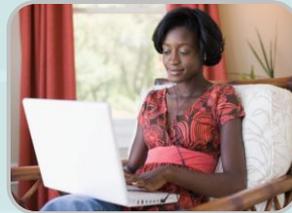
My Clinical Record

Consumers link to their clinical histories with genetic profiles; access clinical research; participate in volunteer networks





Standards



Interoperability



Data Sharing



Connectivity

caGRID

BIG Health Participants to Date



Academic/Health Care Delivery

- Baylor College of Medicine
- Christiana Care Health System
- Duke Comprehensive Cancer Center
- Georgetown University
- MIT Center for Biomedical Innovation
- NCI Community Cancer Centers Program (NCCCP)
- UCSF Breast Care Center

(Bio)Pharmaceutical and Diagnostic

- Genzyme Genetics
- Johnson & Johnson
- Monogram Biosciences

Venture Capital

- Mohr Davidow Ventures

IT/EHR/PHR

- 5AM Solutions
- Cerner Corporation
- HealthCare IT Inc.
- Oracle
- SAS
- Sophic Systems Alliance

Foundations/Non-Profit/Advocacy

- Brookings Institution
- Canyon Ranch Institute
- CollabRx
- Critical Path Institute
- *FasterCures*
- Institute of Medicine
- Kauffman Foundation
- Lance Armstrong Foundation
- Personalized Medicine Coalition

Government

- Cancer Biomedical Informatics Grid® (caBIG®)
- National Cancer Institute (NCI)
- National Office of Public Health Genomics - CDC
- HHS Personalized Health Care Initiative
- Office of the National Coordinator (ONC)

Health Care Consultancy

- Booz Allen Hamilton
- Deloitte Center for Health Solutions
- Feinstein Kean Healthcare

Personal Genomics

- Navigenics
- 23 and Me

Please visit: <https://bighealth.nci.nih.gov/index.php/Participants>

BIG Health Uses 21st Century Communication Channels



The End of a Beginning in Personalized Medicine

September 4, 2008 by kbuetow

The first manuscript reporting results for The Cancer Genome Atlas (TCGA) was published today in the advanced, on-line edition of Nature. TCGA is a 3-year pilot project of the National Cancer Institute (NCI) and the National Human Genome Research Institute (NHGRI) whose goal is to increase our comprehensive understanding of the molecular basis of cancer. The TCGA team describes the discovery of a complex collection of molecular alterations in glioblastoma multiforme (GBM) that have potential implications for the diagnosis and treatment. GBM is the most common form of brain cancer in adults affecting 21,000 people annually.

The paper describes previously unknown high frequency mutations for NF1, ERBB2, and PIK3CA and confirms previous mutational findings in PTEN, RBI, EGFR, and PIK3CA. It implicates three pathways: the CDK/cyclin/CDK inhibitor/RE pathway, the p53 pathway, and the RTK/RAS/PIK pathway as the target of molecular alterations in over 80% of GBMs.

These findings, whose true biologic and clinical significance will only be known over time, are of immediate significance in two ways. First, this novel integration of

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Making Personalized Medicine a Reality.

Contributors **BIGHEALTH** Blog on: CONSORTIUM.

BIG HEALTH OVERVIEW

In this Overview presentation, Dr. Ken Buetow, the BIG Health Catalyst, presents the vision and goals of the BIG Health

Creating the regulatory framework we need

Feb 09, 2009

What is BIG Health?

The BIG Health Consortium™ is a collaboration among stakeholders in biomedicine, including government, academe, industry, non-profit, and consumers, who come together in a novel organizational framework to demonstrate the feasibility and benefits of the personalized medicine paradigm. Through a series of personalized medicine projects, with an expanding number of collaborators, the BIG Health Consortium™ will bootstrap a new approach in which clinical care, clinical research, and scientific discovery are linked.

The BIG Health Consortium™ will demonstrate that:

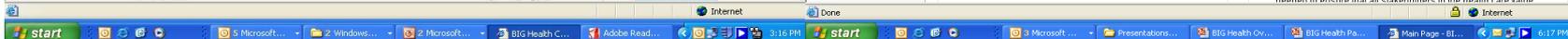
- Loosely-coupled sectors within life sciences and health care can come together in an ecosystem to implement personalized medicine real-work projects, in real time.

What is the status of BIG Health?

The Consortium was initially launched on September 10, 2008 with a kick-off workshop held in Washington, DC. During the meeting, more than 30 stakeholders from academe, government, advocacy, policy, and commerce convened to establish the BIG Health Consortium™ charter and to outline the mission, goals and strategy of the organization. Additionally, two areas were identified as opportunities for action: "Virtual Clinical Research" and a "Learning Healthcare System."

Since that time, the Consortium has convened a number of Action Groups to advance the BIG Health Consortium™ from concept to reality. These groups focus on the following:

- The Communications and Outreach Action Group focuses on the communications policies, strategies, tools and programs needed to ensure that all stakeholders in the health care value



BIG Health Addresses Many of the Prerequisites of a New Biomedical Paradigm



Cost/inefficiency of screening

Builds screening into clinical care

Access to study populations

Draws existing patient base into clinical research

Acceptance in the community

Provides a proactive role for the consumer

Misaligned incentives

Provide alternative business models and partners

Data disconnects

Provides the IT infrastructure to link entire process

Lack of interoperability of research and clinical systems

Provides a ready-made system of interoperability

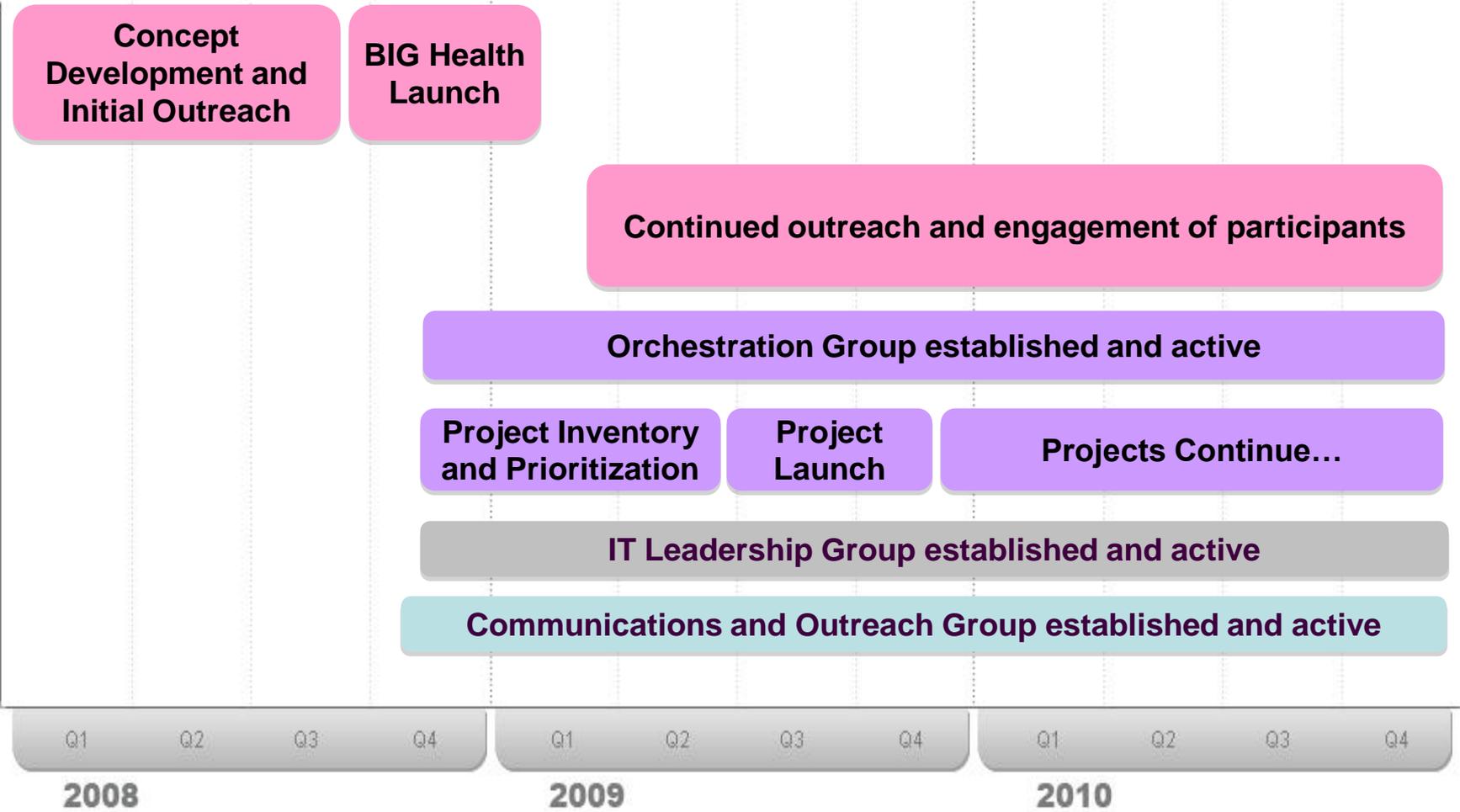
Requirements for systems-level effort that daunt an individual company

Shares the “burden” of transformation

Lack of knowledge among patients and physicians

Provides a pathway for education

BIG Health Planning Timeline



BIG Health Project Evolution Framework

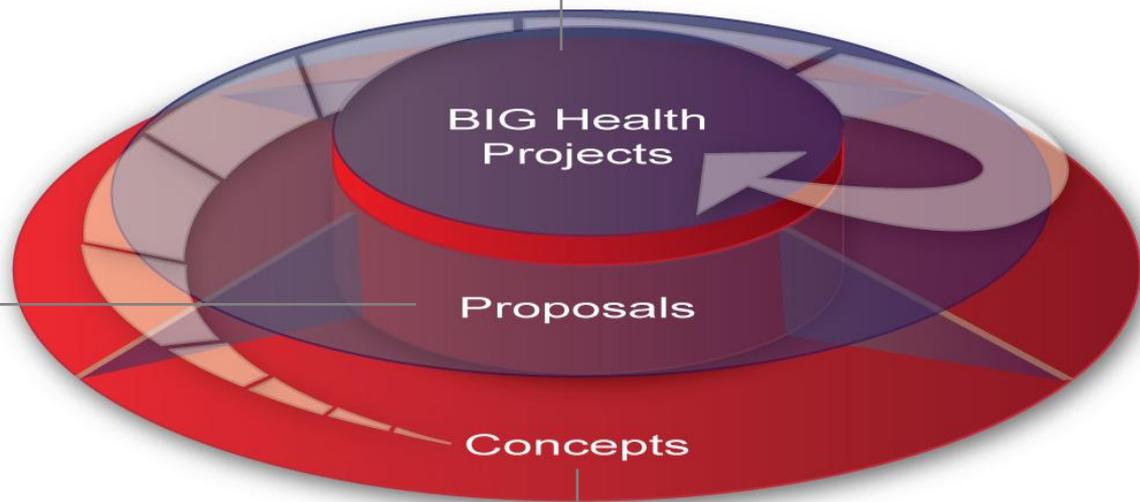
A BIG HEALTH PROJECT is a project or collection of projects purposefully designed to demonstrate or prove a desired outcome that will advance, enable, or support BIG Health's mission in its efforts to promote and accelerate personalized and translational medicine. The results of the BIG Health Project must be quantifiable and tangible.

A PROPOSAL is one or more concepts that have been taken to a deeper level of detail and planning. It involves taking the concept and proposing how it could be achieved and who would be involved to help accomplish the project and documenting this in a formal proposal.

 *Proposal Submission Form (Template)*

A CONCEPT is simply an idea that has been collected during a BIG Health meeting or submitted by a BIG Health Community member. The concept doesn't necessarily have any detail or depth. Think of this as if someone were to say, "wouldn't it be great if..."

 *Concept Submission Document (Template)*



- **“Virtual” Clinical Research**
 - Infrastructure and processes will be engineered to enable individuals to be molecularly-profiled to support clinical research therapeutics, diagnostics, prognostics, so that research can be conducted **without re-inventing the entire infrastructure for every new therapy.**
- **Learning Healthcare System**
 - Activities will be undertaken to demonstrate a learning health care system in which data on health care encounter information are used to assure continuity of care, inform treatment and optimize clinical outcomes, **in a ‘virtuous’ circle of discovery, knowledge, and practice.**

Concepts Under Discussion

- Athena Project “Personalized Breast Health Initiative” (*discussed 2/24/09*)
- Distributed Clinical Trials Recruitment Network (*discussed 1/27/09*)
- Melanoma Trial
- Molecularly Informed Comparative Effectiveness
- Object-Process Methodology
- Patient Reported Outcomes (*discussed 1/23/09*)
- RegistryNXT!

Other proposed Concepts

- ALS Trial Alzheimer's Trial
- Cancer Encounter & Outcomes Repository
- Cancer Survivor Database
- Cardiovascular Pharmacogenomics
- Family Health History Tool
- Hyperlipidemia Study
- NCCCP-wide Encounter Database
- Newborn Screening
- Patient-centric Continuity of Care Portal
- Patient Outcomes Dashboard Quality of Care Database
- Standardized Consumer Data
- Texas Cancer Consortium Study
- Virtual Lung Cancer Trial

The main goals of the Athena “Personalized Breast Health Initiative” concept are to:

- Use data and risk models to develop personalized, evidence-based innovations in the diagnosis and treatment of breast cancer.
- Create an unparalleled biospecimen and data repository to fuel research and clinical innovation in screening, diagnosis and treatment of breast cancer.
- Create results that will lead to innovations in preventing and managing breast cancer.
- Implement a comprehensive informatics strategy that includes innovative tools to collect, analyze and distribute data in real time among all stakeholders.
- Create a model for public/private partnerships to speed delivery and approval of new diagnostics and tailored therapies.

The main goals of Patient Reported Outcomes (PRO) concept are to:

- Demonstrate the integration of PRO data into at least three aspects of cancer research and care: Clinical care; therapeutic and non-therapeutic clinical trials; and tailored patient education
- Provide better evidence on how to treat specific patient concerns, resulting from rigorous scientific demonstration of the effectiveness of new therapeutic strategies and approaches;
- Provide better evidence on how to incorporate current best evidence into whole person models of care;
- Create new methods to support the model:
 - IT platforms and assessment methods that capture the patient's experiences and symptoms (i.e., what matters to the patient and family)
 - Treatment approaches that address a full range of concerns
 - Methods for monitoring outcomes, broadly defined
 - Quality assurance metrics and processes that encompass new parameters
 - Mechanisms for follow-up with patients over time

Criteria for Projects

- Multi-stakeholder community
- Multi-institutional engagement
- Regional/National/International in scope
- Extensible
- Pathway to sustainability

Activities underway...

- All materials are available at BIG Health wiki (<http://bighealth.nci.nih.gov>)
- BIG Health participant capabilities are continuously gathered (<https://bighealth.nci.nih.gov/index.php/Capabilities>)
- A portfolio of potential concepts and projects are being compiled
- Concepts are discussed during Project Action Group (PAG) meetings <https://bighealth.nci.nih.gov/index.php/Concepts>
 - Athena Project “Personalized Breast Health Initiative” - discussed 2/24/09
 - Distributed Clinical Trials Recruitment Network - discussed 1/27/09
 - Patient Reported Outcomes - discussed 1/23/09
- Action Groups are meeting to plan for protocols, resources, etc.
- Initial selection of projects by Q1’09
- Projects ready for launch by Q2’09

How BIG Health Participation Works



- Attend Action Group Meetings
 - **Project Action Group** (PAG)
 - **Orchestration Action Group** (OAG)
 - **Communications and Outreach Action Group**
 - **IT Leadership Group**
 - Check the wiki for upcoming meeting dates/times at <http://bighealth.nci.nih.gov/>
- Use BIG Health Web 2.0 capabilities and communications tools (<http://www.bighealthconsortium.org/about/getinvolved/>)
 - Submit a personal/organizational profile for inclusion on the site
 - Submit concepts or project proposal ideas on the Website or wiki
 - Join mailing list and alert peers/colleagues to upcoming meetings
 - Post comments through the BIG Health Consortium™ blog

Not sure of your role or next step?

Contact connector@bighealthconsortium.org for more information

BIG Health will help you...

- Enhance your activities
- Help fulfill your mission
- Provide missing components to accelerate your programs
- Connect to potential partners



BIG Health participants provide...

- 
- Novel and exciting project ideas that enable personalized medicine
 - Capabilities and resources to help progress BIG Health projects
 - Thought leadership and best practices

Framework for Action



Think big...
Start small...
Act now!

- **Project Action Group Discussion Forum: Molecularly Informed Comparative Effectiveness**
 - Friday, March 20th, 12-1 EDT
 - *Dial-in: 1-877-327-4956 Passcode: 3965087*
 - Centra: <http://mt202.centra.com/main/Customers/ncicb>
 - Event ID: PAG Discussion
- **April Communications and Outreach Action Group meeting**
 - Wednesday, April 15th, 4-5 EDT
 - *Dial-in: 1-877-327-4956; Passcode: 3965087*
 - Centra: <http://mt202.centra.com/main/Customers/ncicb>
 - Event ID: communication
- **Other activities**
 - Guest blogs
 - Submitting profiles and capabilities through our online forms, found at: <http://www.bighealthconsortium.org/about/getinvolved/>

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For more information, contact:
[**connector@BIGHealthConsortium.org**](mailto:connector@BIGHealthConsortium.org)